REMARKS

Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 35, 39, 46-48, 53, 60, 66, 67, and 70 to 73 were pending in the present application. Claims 35, 39, 46-48, 53, 60, and 66 are withdrawn from consideration. Claims 1, 4, and 67 have been amended to substitute the definite article for the indefinite article as suggested by the Examiner. Since the existence of a complementary sequence is an inherent property of a polynucleotide sequence, no literal antecedent basis for complementary polynucleotide is required. Claim 67 has further been amended to eliminate SEQ ID NOs:15-19 from the proviso.

New claims 74 to 75 have been added. Support for the new claims can be found in the specification as originally filed as set forth in the chart below.

Claim	Support
74	¶12
75	¶13; ¶63
76	¶13

No new matter has been introduced. Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 35, 39, 46-48, 53, 60, 66, 67, and 70 to 76 are pending in the present application upon entry of the present amendment.

Change of Attorney Docket Number

Applicants direct the Examiner's attention to the new attorney docket number for this case, which is **7682-135-999**. Applicants request that the Office's records be updated to reflect the change in the attorney docket number.

The Rejections under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 1, 2, 4, 6, 10, 11, 12, 14, 15, 16, 19, 20, 67, and 70-73 is rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. In particular, the claims have been rejected because the phrase "a complementary polynucleotide thereof" could include fragments.

In response, claims 1, 4, and 67 have been amended to substitute the definite article for the indefinite article as suggested by the Examiner. Claims 2, 6, 10, 11, 12, 14, 15, 16, 19, 20, and 70-73 depend, directly or ultimately, from claims 1, 4, or 67, respectively. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, for indefiniteness, should be withdrawn.

The Rejections under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1, 2, 4, 6, 10, 11, 12, 14, 15, 16, 19, and 20 are rejected under 35 U.S.C. § 112, first paragraph, for insufficient written description. Applicants disagree as set forth in detail below.

Among others, Applicants had previously argued that the claimed viruses are identified structurally, namely by sequence homology, and functionally, namely by the ability of the encoded virus to be infectious and replicating. In addition, at the time the instant application was filed, there was a known correlation between structure and function. Specifically, structure-function analyses had been published on homologous viral sequences such that the skilled artisan at the time the application was filed would have known which sequences can and which cannot be modified to obtain infectious and replicating viruses. To support their argument, Applicants had provided scientific publications demonstrating the known correlation between structure and function for the F gene, the G gene, and promoters of RSV. In response, the Examiner contended that modifications in regions other than the F and the G gene are encompassed by the claims and concluded that Applicants' evidence was insufficient to demonstrate a known correlation between structure and function over the entire viral genome of SEQ ID NO:1.

Applicants present additional evidence herein to establish that a structure function relationship was well-established in the art for each of the ORF's of RSV, including N, P, M, F, SH, G and L. Applicants submit additional references to further demonstrate that in addition to the RSV F and G genes, a structure function relationship had been established between RSV genomes and the encoded viral proteins. Van den Hoogen *et al.*, 2002 (Virology 295:119-132; "van den Hoogen"; attached as Exhibit A) conducted comparisons of the amino acid sequences of the viral proteins among different members of the *Paramyxoviridae* family, including strains of human RSV subgroups A (hRSV A) and B (hRSV B). These alignments reveal blocks of high conservation in *multiple* ORFs (*e.g.*, in N, P, and L; see Figures 2, 3, and 9); conserved peptides (*e.g.*, in M; see Figure 4) and

multiple single amino acid positions that are conserved (*e.g.*, the cysteines in F and M2-1; see Figures 5 and 6A). Moreover, other identifying characteristics, such as the conserved hydrophobicity profile of the SH and G ORFs were identified. The functional importance of these conserved regions is discussed in van den Hoogen. For example, the conserved region of the phosphoprotein is likely to be required for replication of the genome. The four conserved motifs of domain III of the polymerase are also likely required for replication. Applicants provide as Exhibit B Stec *et al.*, 1991 (Virology 183:273-287; "Stec"), which presents a comparison of the L proteins of RSV and other paramyxoviruses, in order to define sequences that represent conserved regions. Thus, the skilled artisan, by aligning the sequence of RSV B 9320 to the van den Hoogen and Stec alignments, would know which portions of these ORFs are conserved and therefore are functionally or structurally important and should be maintained and which portions could be deleted or mutated while retaining viral function.

Similarly, the Examiner had found unpersuasive Applicants' analogy between the present case and the facts of *Invitrogen v. Clontech*, 429 F.3d 1052 (Fed. Cir. 2005; attached as Exhibit A) because the claims-in-suit in *Invitrogen* related to a single protein whereas the present claims are directed, among others, to nucleic acids encoding an infectious, replicating virus. Applicants assert that this difference does not detract from the applicability of *Invitrogen*'s proposition that a known correlation between structure and function need not be disclosed to the present situation. In fact, the only difference is that the viral genome encodes multiple proteins. For each gene, however, a known correlation between structure and function exists as discussed above. The fact that the individual proteins are ultimately assembled into an infectious, replicating virus also does nothing to distinguish the present situation from *Invitrogen*. For example, sequence alignments reveal the conserved elements that are functionally relevant for infectivity and replication of the virus. In fact, the Federal Circuit vacated a holding of the Board of Patent Appeals and Interferences ("the Board") that claims directed to chimeric genes which once transfected into a cell trigger activation and/or proliferation of the cell were not sufficiently described. *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005). In *Capon*, the inventions were directed to chimeric genes formed from combinations of known DNA segments. The Board of Patent Appeals and Interferences ("the Board") rejected Applicant's claims for lack of written description because the specification at issue did not include the complete nucleotide sequence of at least one chimeric gene exemplary of the claimed genus. *Id.* at 1356. The Federal Circuit vacated the Board's holding, explaining that, because the invention does not concern the discovery of gene function or structure, and rather concerns novel chimeric genes prepared from DNA segments

of known structure and function, the specification need not recite specific sequences in order to satisfy the written description requirement. *Id.* at 1360-1361.

The above examples illustrate that the skilled artisan was familiar with the structural basis of different aspects of RSV viral functions at the time the application was filed. Thus, the correlation between structure and function was well-known in the art.

In view of the high skill in the art, once provided with the viral genomic sequence of RSV B 9320 coupled with the identified percentages of sequence identity, and functional characteristics, one skilled in the art would be able to practice the claimed invention without the recitation of each and every claimed sequence.

Because the factual situation in *Invitrogen* is very similar to the present situation and because the rational the led to the holding in *Invitrogen* squarely applies to the present case, Applicants request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicants respectfully submit that all of the pending claims are now in condition for allowance. If there are any remaining concerns, the Examiner is invited to call the undersigned to schedule an interview.

It is believed that no fee is due in connection with this Amendment other than that for the extension of time; however, in the event any additional fee is required, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted, by: Jacqueline Benn
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Date: May 25, 2007

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